

AMENDMENTS TO THE CLAIMS:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1.-15. (Canceled)

16. (Canceled)

17. (Currently Amended) A method of identifying a small molecule that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

- (a) contacting a region of human 28S rRNA with a library of small molecules under conditions that permit direct binding of the region of human 28S rRNA to a member of the library of small molecules and the formation of a region of human 28S rRNA:small molecule complex;
- (b) detecting the formation of a region of human 28S rRNA:small molecule complex, wherein a small molecule that binds to the region of human 28S rRNA is identified if a region of human 28S rRNA:small molecule complex is detected;
- (c) contacting the small molecule identified as binding to a region of human 28S rRNA with a cell-free extract and containing a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene coding region, wherein the reporter gene coding region comprises a premature stop codon, and wherein the cell-free extract is isolated from cells that have been incubated on ice for at least 12 hours; and
- (d) detecting the protein expressed from the reporter gene coding region, wherein a small molecule that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the protein expressed from the reporter gene coding region in the presence of the small molecule is altered relative to the protein expressed from the reporter gene coding region in the absence of the small molecule or the presence of a negative control.

18. (Currently Amended) A method of identifying a small molecule that modulates premature translation termination or nonsense-mediated mRNA decay, said method comprising:

- (a) contacting a region of **human 28S rRNA** with a library of small molecules under conditions that permit direct binding of the region of human 28S rRNA to a member of the library of small molecules and the formation of a region of human 28S rRNA:small molecule complex;
- (b) detecting the formation of a region of human 28S rRNA:small molecule complex, wherein a small molecule that binds to the region of human 28S rRNA is identified if a region of human 28S rRNA:small molecule complex is detected;
- (c) contacting the small molecule identified as binding to a region of human 28S rRNA with a cell-free extract and a nucleic acid sequence comprising a regulatory element operably linked to a reporter gene coding region, wherein the reporter gene coding region comprises a premature stop codon, and wherein the cell-free extract is isolated from cells that have been incubated on ice for at least 24 hours; and
- (d) detecting the protein expressed from the reporter gene coding region, wherein a small molecule that modulates premature translation termination or nonsense-mediated mRNA decay is identified if the protein expressed from the reporter gene coding region in the presence of the small molecule is altered relative to the protein expressed from the reporter gene coding region in the absence of the compound or the presence of a negative control.

19. (Currently Amended) The method of claim ~~46~~, 17 or 18 wherein the region of human 28S rRNA is detectably labeled.

20. (Currently Amended) The method of claim ~~46~~, 17 or 18, wherein the small molecules in the library are detectably labeled.

21. (Canceled)

22. (Currently Amended) The method of claim 17 or 18, wherein the cell-free extract is from human cells.

23. (Currently Amended) The method of claim 17 or 18, wherein the cell-free extract is rabbit reticulocyte lysate or wheat germ extract.

24. (Currently Amended) The method of claim 17 or 18, wherein the cell-free extract is a cell free extract from HeLa cells.

25. (Canceled)

26. (Canceled)

27. (Currently Amended) The method of claim ~~18 or 22~~, wherein the cell-free extract is a S10 to S30 cell-free extract.

28. (Currently Amended) The method of claim 22 25, wherein the cell-free extract is a S10 to S30 cell-free extract.

29. (Currently Amended) The method of claim 17 26, wherein the cell-free extract is a S10 to S30 cell-free extract.

30. (Currently Amended) The method of claim ~~18 or 22~~, wherein the cell-free extract is a S5 to S25 cell-free extract.

31. (Currently Amended) The method of claim 22 25, wherein the cell-free extract is a S5 to S25 cell-free extract.

32. (Currently Amended) The method of claim 17 26, wherein the cell-free extract is a S5 to S25 cell-free extract.

33. (Previously Presented) The method of claim 30, wherein the cell-free extract is a S10 cell-free extract.

34. (Previously Presented) The method of claim 31, wherein the cell-free extract is a S10 cell-free extract.

35. (Previously Presented) The method of claim 32, wherein the cell-free extract is a S10 cell-free extract.

36. (Canceled)

37. (Currently Amended) The method of claim ~~46~~, 17 or 18, wherein the region of human 28S rRNA comprises a region involved in frameshifting, nonsense mutation suppression, GTPase activity, or peptidyl transferase activity.

38. (Currently Amended) The method of claim ~~46~~, 17, or 18, wherein each small molecule in the library is attached to a solid support.

39. (Previously Presented) The method of claim 38, wherein the solid support is a silica gel, a resin, a derivatized plastic film, a glass bead, cotton, a plastic bead, a polystyrene bead, an aluminum gel, a glass slide or a polysaccharide.

40. (Currently Amended) The method of claim ~~46~~, 17 or 18, wherein the library of small molecules is attached to a chip.

41. (Previously Presented) The method of claim 19, wherein the detectably labeled region of human 28S rRNA is labeled with a fluorescent dye, phosphorescent dye, ultraviolet dye, infrared dye, visible dye, radiolabel, enzyme, spectroscopic colorimetric label, affinity tag, or nanoparticle.

42. (Previously Presented) The method of claim 20, wherein the detectably labeled small molecules in the library are labeled with a fluorescent dye, phosphorescent dye, ultraviolet dye, infrared dye, visible dye, radiolabel, enzyme, spectroscopic colorimetric label, affinity tag, or nanoparticle.

43. (Currently Amended) The method of claim ~~46~~, 17 or 18, wherein the small molecule library is a library of benzodiazepines, isoprenoids, thiazolidinones, metathiazanones, pyrrolidines, morpholino compounds, or diazepindiones.

44. (Currently Amended) The method of claim ~~46~~, 17 or 18, wherein the detectably labeled region of human 28S rRNA:small molecule complex is detected by electrophoresis, fluorescence spectroscopy, surface plasmon resonance, mass spectrometry, scintillation, proximity assay, structure-activity relationships (“SAR”) by NMR spectroscopy, size exclusion chromatography, affinity chromatography, or nanoparticle aggregation.

45. (Currently Amended) The method of claim ~~46~~, 17 or 18, wherein the method further comprises determining the structure of the small molecule.

46. (Previously Presented) The method of claim 45, wherein the structure of the small molecule is determined by mass spectroscopy, NMR, X-ray crystallography, Edman degradation or vibration spectroscopy.

47. (Previously Presented) The method of claim 17 or 18, wherein the premature stop codon is UAG, UGA or UAA.

48. (Previously Presented) The method of claim 17 or 18, wherein the premature stop codon ~~that~~ is in the context of UAAG, UAAA, UAGG, UAGC, UAGU, UAAC, UGAC, or UAAU.

49. (Currently Amended) The method of claim 17 or 18, wherein the reporter gene coding region contains 2 or more premature stop codons.

50. (Previously Presented) The method of claim 17 or 18, wherein an increase in the amount of protein expressed in the presence of the small molecule relative to the amount of protein expressed in the absence of the small molecule or the presence of a negative control indicates that the small molecule suppresses premature translation termination or nonsense-mediated mRNA decay.

51. (Previously Presented) The method of claim 17 or 18, wherein a decrease in the amount of protein expressed in the presence of the small molecule relative to the amount of protein expressed in the absence of the small molecule or the presence of a negative control indicates that the small molecule enhances premature translation termination or nonsense-mediated mRNA decay.

52. (New) The method of claim 17 or 18, wherein the region of human 28S rRNA comprises domains II and V.